UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,415	01/16/2004	William S. Brusilow	2930-109	5654

6449 7590 02/18/2010

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
VAKILI, ZOHREH	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/18/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/758,415	BRUSILOW, WILLIAM S.	
	Examiner	Art Unit	
	ZOHREH VAKILI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6-9 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,10,11 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are presented for examination.

Applicant's Amendment filed November 10, 2009 has been received and entered into the present application. Claims 6-9 and 12-20 are withdrawn from further consideration. Claims 1-5, 10, 11, and 21 are pending and are herein examined on the merits.

Applicant's arguments, filed November 10, 2009 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (Maintained)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 10-11, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Apostolakis et al., Brain Research Bulletin, or Ginefri-Gayet et al., Pharmacology Biochemistry and Behavior, in view of Liedtke et al. (US Pub. No. 20030013650 A1), and further in view of Feurerstein et al. (US Pub. No. 20020173537 A1).

Apostolakis teaches methionine sulfoximine (MSO) is a centrally acting neurotoxin with convulsive properties; it has been used in study of epilepsy. MSO suppresses the formation of glutamine (see page 257, col. 1, first paragraph). Apostolakis further teaches pharmaceutical unit doses in an amount of methionine sulfoxime of 2 mg/ml normal saline and 200 micro gram/100 micro liter administered intravenously (IV) and intracerebroventricularly (IVT). The animals were sacrificed at different times after MSO administration (see page 257, column 2).

Ginefri-Gayet teaches pharmaceutical unit doses in an amount of methionine sulfoxime of 50-75 micro gram/10 micro liters. See page 174, column 2, under ICV Injection of MSO.

Liedtke teaches that the present invention relates to the identification in vertebrate animals including humans, of an ion channel for rapid conduction of cations, among them, Ca^{2+}. This ion channel, named VR-OAC, demonstrates activity as an osmoreceptor, and also demonstrates a role in mechanical stimulation and responsiveness (see page 1, paragraph 2). VR-OAC is expressed in nerve-cells of the hippocampus, CAI region, a region of importance for memory and in epileptic seizures (page 6, paragraph 89). Liedtke further teaches that the recombinant protein can be

refolded prior to or after cleavage to form a functionally active polypeptide. Suitable redox (reducing/oxidizing) agent pairs include, but are not limited to, reduced glutathione/glutathione disulfide, cystine/cysteine, cystamine/cysteamine (see page 16, paragraph 203). Mammalian expression vectors contemplated for use in the invention include vectors with inducible promoters, such as, a glutamine synthetase/methionine sulfoximine co-amplification vector, (see page16, paragraph 207), which reads on claims 10 and 11.

Feurerstein et al. teach of a compound treating neurodegenerative diseases including polyglutamine diseases (see page 1, paragraph 0003). The composition is useful for treating a polyglutamine disease e.g. Huntington's disease, dentorubropallidoluysian atrophy, spinal and bulbar muscular atrophy, spinocerebellar ataxis (SPA -1, -2, -3, -6, -7), and acute and chronic glaucoma. Also the compounds are useful for treating disorders of central nervous system e.g. stroke, hypoglycemia, hypoxia, trauma, epilepsy, Alzheimer's disease, AIDS-associated dementia, amyotrophic lateral sclerosis, Parkinson's disease and chronic alcoholism (see page 2, paragraph 0030).

Clearly, the skilled artisan is provided with ample instruction and motivation to use MSO in the treatment of neurodegenerative diseases including polyglutamine diseases. The skilled artisan is motivated to make compositions of the well known ingredients used in applications for treatment of polyglutamine diseases. The prior art teach of the same component and its concentration that is instantly claimed. Accordingly, it is well settled that products of identical chemical composition cannot

have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure that is used to treat one disease, therefore will treat another disease from the same family as taught by Feurerstein et al., the properties applicant discloses and/or claims are necessarily present. In other words, where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. See In reBest, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach and suggest the invention as claimed. Thus the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and was as a whole, *prima facie* obvious.

Thus in the absence of evidence to the contrary, the invention of claims 1-5, 10-11, and 21 would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Response to Argument

Applicant argues that Apostolakis does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, and spinobulbar muscular atrophy and in view of the undesirable side effects

discussed in Apostolakis (i.e. convulsions, deformation, atrophy, loss of striation of muscle fibers, fibrosis and degeneration of Purkinje cells in the cerebellum). Ginefri-Gayet does not cure the deficiencies in Apostolakis as Ginefri-Gayet discloses that MSO, when administered at a convulsant dose (100-200 mg/kg body weight administered intraperitonealy or 50-75 micro g per rat administered by ICV injection) induces a decrease in body temperature. Ginefri-Gayet does not suggest or disclose that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy and in view of the undesirable side effect (hypothermia). Applicants are unclear as to how Liedtke is related to the presently claimed invention. In any case, Liedtke does not cure the deficiencies in Apostalakis and Ginefri-Gayet as Liedtke does not suggest or disclose that MSO can be used to treat polyglutamine diseases. Feurerstein is directed to a method for treating a polyglutamine disorder using 2- pyrrolidinone derivatives. Feurerstein does not teach the use of MSO and thus does not cure the deficiencies in Apostalakis, Ginefri-Gayet and Liedtke as discussed above. None of the cited references alone or in combination suggest that MSO can be used to treat polyglutamine diseases such as Huntington's disease, spinocerebellar ataxia, or spinobulbar muscular atrophy and in view of the side effects disclosed in the prior art, one skilled in the art would not be motivated to test MSO for the treatment of such diseases.

Examiner traverses Applicant's arguments Apostolakis teaches methionine sulfoximine (MSO) is a centrally acting neurotoxin with convulsive properties; it has been used in study of epilepsy. MSO suppresses the formation of glutamine. As

evidenced by Feurerstein et al. that teach of a compound treating neurodegenerative diseases including polyglutamine diseases (see page 1, paragraph 0003). The composition is useful for treating a polyglutamine disease e.g. Huntington's disease, dentorubropallidoluysian atrophy, spinal and bulbar muscular atrophy, spinocerebellar ataxis (SPA -1, -2, -3, -6, -7), and acute and chronic glaucoma. Also the compounds are useful for treating disorders of central nervous system e.g. stroke, hypoglycemia, hypoxia, trauma, epilepsy, and Alzheimer's disease (see page 2, paragraph 0030). The compound that is used in the treatment of epilepsy is also beneficial in the treatment of polyglutamine diseases as been taught by Feurerstein et al. (see page 1, paragraph 0003 & page 2, paragraph 0030). The characteristics and properties of the composition are inseparable from each other. If the same compound has a deficiency or benefits in one composition will have the same deficiency or benefits in another composition. Claims 10 and 11 are directed to the method according to claim 1, further comprising administering a second compound which inhibits aggregate formation, inhibits transglutaminase, inhibits caspase, or is neuroprotective, wherein said second compound is selected from the group consisting of Congo red, cystamine, cysteamine, minocycline, ethyl eicosapentaenoate, and riluzole. Liedtke teaches suitable redox (reducing/oxidizing) agent pairs include, but are not limited to, reduced glutathione/glutathione disulfide, cystine/cysteine, **cystamine/cysteamine** (see page 16, paragraph 203). Mammalian expression vectors contemplated for use in the invention include vectors with inducible promoters, such as, a glutamine synthetase/methionine sulfoximine co-amplification vector. Applicant's remarks have

been fully and carefully considered in their entirety, but fail to be persuasive. Applicant is reminded that the obviousness rejection is not an anticipation rejection. The above mentioned references clearly teach the use of MSO in treating polyglutamine diseases, and its concentration. In obviousness rejection a combination of references is used, and the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references that make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the combination of the cited references. *In re Young*, 403 F.2d 754, 159 USPQ 725(CCPA 1968); *In re Keller 642 F.2d 413, 208 USPQ 871 (CCPA 1981).*

Moreover, it is noted that rejections under 35 U.S.C. 103(a) are based on combinations of references, where the secondary references are cited to reconcile the deficiencies of the primary reference with the knowledge generally available to one ordinary skill in the art to show that the differences between Applicant's invention and the prior art are such that they would have been modifications that were *prima facie* obvious to the skilled artisan. It is noted that the claimed invention is not required to be expressly suggested in its entirety by any one or all of the references cited under 35 U.S.C. 103(a). Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Applicant has not overcome the rejection. Applicant's remarks have been fully and carefully considered in their entirety, but fail to be persuasive in establishing error in the propriety of the present rejection.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zohreh Vakili whose telephone number is 571-272-3099. The examiner can normally be reached on 8:30-5:00 Mon.-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Zohreh Vakili

Patent Examiner 1614 January 26, 2010

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614